

PHYTOCHEMICAL AND PHARMACOLOGICAL REVIEW ON ANDROGRAPHIS PANICULATA

Abhishek Chowdhury*, Asutosh Banerjee and Dr. Beduin Mahanti

School of Pharmacy, Techno India University, Salt Lake City, Sector-V, EM:4/1, Kolkata – 700091, West Bengal, India.



*Corresponding Author: Abhishek Chowdhury

School of Pharmacy, Techno India University, Salt Lake City, Sector-V, EM:4/1, Kolkata – 700091, West Bengal, India.

Article Received on 21/04/2024

Article Revised on 11/05/2024

Article Accepted on 01/06/2024

ABSTRACT

Andrographis paniculata, commonly known as "King of Bitters," is a medicinal plant widely used in traditional medicine systems across Asia. This review paper aims to provide a comprehensive overview of the ethnobotany, phytochemistry, pharmacology, and clinical applications of *A. paniculata*. The plant is rich in bioactive compounds, with andrographolide being the most abundant and extensively studied constituent. *A. paniculata* exhibits a wide spectrum of pharmacological activities, including hepatoprotective, immunostimulatory, antipyretic, antioxidant, antidiabetic, anti-inflammatory, antibacterial, antiviral, and anticancer effects. These properties are attributed to the presence of various phytochemicals, such as diterpenoids, flavonoids, and polyphenols. The review also discusses the safety, toxicology, and potential side effects of *A. paniculata*, as well as the different formulations and standardization techniques employed for its preparations. Despite the extensive research on *A. paniculata*, further studies are needed to fully understand its mechanisms of action, pharmacokinetics, and clinical efficacy. This review highlights the potential of *A. paniculata* as a promising therapeutic agent and identifies areas for future research and development.

KEYWORDS: The plant is rich in bioactive compounds, with andrographolide being the most abundant and extensively studied constituent.

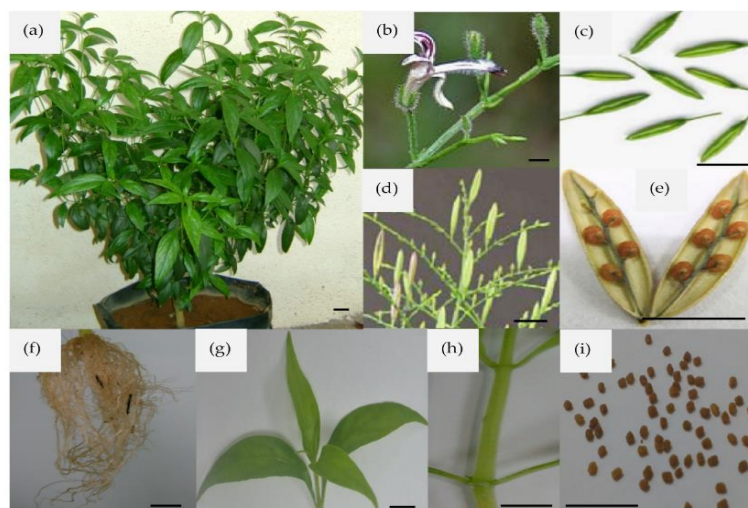


Figure 1: Andrographis paniculata and its different parts. (a) Aerial part, (b) flower, (c) pod stage with panicles: mature capsule, (d) fruit, (e) opened capsule, (f) roots, (g) leaves: opposite arrangement, (h) stem, and (i) seed. Bar = 1 cm.

INTRODUCTION

Andrographis paniculata, belonging to the family Acanthaceae, is a medicinal plant widely distributed in tropical and subtropical regions of Asia, particularly in India, China, and Southeast Asian countries.^[1] The plant

is commonly known as "King of Bitters," "Kalmegh," or "Chuanxinlian" due to its intensely bitter taste.^[2] *Andrographis paniculata* has been used for centuries in traditional medicine systems, such as Ayurveda, Siddha, and Traditional Chinese Medicine, for the treatment of

various ailments, including respiratory infections, fever, digestive disorders, and skin diseases.^[3,4]

The aerial parts of *Andrographis paniculata*, particularly the leaves and stems, are the most commonly used parts for medicinal purposes.^[5] The plant is rich in bioactive compounds, with the major constituents being diterpenoids, flavonoids, and polyphenols.^[6] Among these, andrographolide, a bicyclic diterpenoid lactone, is the most abundant and extensively studied compound, known for its wide range of pharmacological activities.^[7]

Numerous studies have investigated the phytochemistry, pharmacology, and clinical applications of *Andrographis paniculata*, revealing its potential as a therapeutic agent for various diseases.^[8] The plant exhibits a wide spectrum of pharmacological activities, including hepatoprotective, immunostimulatory, antipyretic, antioxidant, antidiabetic, anti-inflammatory, antibacterial, antiviral, and anticancer effects.^[9,10] These properties are attributed to the presence of bioactive compounds, which act through multiple mechanisms of action, such as modulation of immune responses, inhibition of pro-inflammatory pathways, and regulation of gene expression.^[11]

Despite the extensive research on *Andrographis paniculata*, there is a need for a comprehensive review that summarizes the current knowledge on its ethnobotany, phytochemistry, pharmacology, and clinical applications. This review paper aims to bridge this gap by providing a detailed overview of the various aspects of *Andrographis paniculata*, focusing on its pharmacological activities, safety, and formulations.

The review begins with a discussion on the ethnobotanical significance and traditional uses of *Andrographis paniculata*, followed by a detailed description of its phytochemistry, with a focus on the major bioactive compounds. The subsequent sections explore the various pharmacological activities of *Andrographis paniculata*, including hepatoprotective, immunostimulatory, antipyretic, antioxidant, antidiabetic, anti-inflammatory, antibacterial, antiviral, and anticancer effects. The safety, toxicology, and potential side effects of *Andrographis paniculata* are also addressed, along with the different formulations and standardization techniques employed for its preparations.

This comprehensive review provides valuable insights into the medicinal properties and therapeutic potential of *Andrographis paniculata*, underlining its significance as a medicinal plant of great importance. The review also serves as a foundation for future research and development of *Andrographis paniculata*-based therapeutics, encouraging further exploration of its pharmacological activities and clinical applications.

Literature Review of *Andrographis paniculata*

Hossain *et al.* (2014) gave a comprehensive review of the ethnobotany, phytochemistry, and pharmacology of *Andrographis paniculata*. The authors discussed the traditional uses of *Andrographis paniculata* in various medicinal systems, highlighting its use in the treatment of respiratory infections, fever, digestive disorders, and skin diseases. The review also detailed the phytochemical constituents of *Andrographis paniculata*, focusing on the major bioactive compounds, such as andrographolide, neo andrographolide, and 14-deoxy-11,12-didehydroandrographolide. The pharmacological activities of *Andrographis paniculata*, including its hepatoprotective, immunostimulatory, antipyretic, antioxidant, antidiabetic, anti-inflammatory, antibacterial, antiviral, and anticancer effects, were extensively discussed. The authors provided insights into the mechanisms of action of *Andrographis paniculata* and its constituents, as well as their potential therapeutic applications, while highlighting the need for further research on clinical efficacy, safety, and standardization of *Andrographis paniculata*-based formulations.

Jayakumar *et al.* (2013) suggested that experimental and clinical pharmacology of *Andrographis paniculata* and its major bioactive compound, andrographolide. The authors comprehensively discussed the plant's anti-inflammatory and immunomodulatory effects, attributing them to the inhibition of pro-inflammatory enzymes, cytokines, and transcription factors by andrographolide and other constituents. The review also highlighted the antioxidant properties of *Andrographis paniculata* and its role in protecting against oxidative stress-induced diseases. The potential of *Andrographis paniculata* in managing diabetes and its complications, as well as its cardiovascular and neuroprotective effects, were examined. Additionally, the authors evaluated the anticancer activities of *Andrographis paniculata*, including its ability to induce apoptosis, inhibit proliferation, and suppress angiogenesis in various cancer cell lines and animal models. The review also assessed the clinical evidence for the plant's efficacy in treating respiratory infections, HIV, and cancer.

Chao and Lin (2010) suggested on the isolation and identification of bioactive compounds in *Andrographis paniculata*. The authors provided a detailed account of the various phytochemical constituents of the plant, including diterpenoids, flavonoids, and polyphenols. The review discussed the extraction, purification, and structural elucidation techniques employed in the identification of these bioactive compounds. The authors also highlighted the pharmacological activities of the isolated compounds, with a particular emphasis on andrographolide, the most abundant and extensively studied constituent of *Andrographis paniculata*. The review provided valuable insights into the structure-activity relationships of the bioactive compounds and their potential therapeutic applications in the treatment of

various diseases, such as cancer, diabetes, and inflammatory disorders.

Mishra *et al.* (2007) suggested a comprehensive review of *Andrographis paniculata*, covering its botanical description, traditional uses, phytochemistry, pharmacological activities, and clinical applications. The authors discussed the morphological characteristics and geographical distribution of the plant, as well as its traditional uses in various medicinal systems. The review provided a detailed account of the phytochemical constituents of *Andrographis paniculata*, including diterpenoids, flavonoids, and polyphenols, along with their structures and pharmacological properties. The authors extensively discussed the pharmacological activities of *Andrographis paniculata*, such as its hepatoprotective, immunostimulatory, antipyretic, antioxidant, antidiabetic, anti-inflammatory, antibacterial, antiviral, and anticancer effects, citing relevant *in vitro* and *in vivo* studies. The review also highlighted the clinical applications of *Andrographis paniculata* in the treatment of respiratory infections, HIV, and cancer, as well as its potential as a chemo preventive agent.

Akbar *et al.* (2011) suggested a comprehensive review of the pharmacological activities and clinical effects of *Andrographis paniculata*. The author discussed the traditional uses of the plant in various medicinal systems and its current therapeutic applications. The review detailed the phytochemical constituents of *Andrographis paniculata*, focusing on the major bioactive compounds, such as andrographolide, neo andrographolide, and 14-deoxy-11,12-didehydroandrographolide. The author extensively discussed the pharmacological activities of *Andrographis paniculata*, including its hepatoprotective, immunostimulatory, antipyretic, antioxidant, antidiabetic, anti-inflammatory, antibacterial, antiviral, and anticancer effects, citing relevant *in vitro*, *in vivo*, and clinical studies. The review also examined the clinical efficacy of *Andrographis paniculata* in the treatment of respiratory infections, HIV, and cancer, as well as its potential as an adjuvant therapy. The author highlighted the need for further research to establish the optimal dosage, safety, and long-term efficacy of *Andrographis paniculata*-based formulations.

Puri *et al.* (1993) suggested the immunostimulant agents from *Andrographis paniculata*. The authors isolated and characterized four compounds, namely andrographolide, neo andrographolide, 14-deoxy-11,12-didehydroandrographolide, and 14-deoxyandrographolide, from the ethanol extract of the plant. The immunostimulant activity of these compounds was evaluated using various *in vitro* and *in vivo* assays, such as the phagocytosis of carbon particles by macrophages, the proliferation of splenic lymphocytes, and the activation of natural killer cells. The study revealed that andrographolide and neo andrographolide exhibited significant immunostimulant activity,

enhancing the phagocytic activity of macrophages and the proliferation of lymphocytes. The authors suggested that these compounds could be responsible for the immunostimulant properties of *Andrographis paniculata* and its traditional use in the treatment of infectious diseases.

Sheeja and Kuttan *et al.* (2007) suggested the immunomodulatory effects of *Andrographis paniculata* extract and andrographolide on cytotoxic T lymphocyte (CTL) responses and tumor growth *in vivo*. The study employed a mouse model of melanoma, wherein the animals were treated with either *Andrographis paniculata* extract or andrographolide. The authors observed a significant increase in CTL activity and a reduction in tumor growth in the treated animals compared to the control group. The study also revealed that the treatment enhanced the production of interferon-gamma and interleukin-2, which are crucial for the activation and proliferation of CTLs. The authors suggested that the immunomodulatory effects of *Andrographis paniculata* and andrographolide could be attributed to their ability to stimulate the production of cytokines and activate CTL responses, making them potential candidates for cancer immunotherapy.

Woo *et al.* (2008) studied the protective effects of andrographolide on cardiomyocytes against hypoxia/reoxygenation injury. The authors employed an *in vitro* model of rat cardiomyocytes subjected to hypoxia/reoxygenation stress and treated with andrographolide. The study revealed that andrographolide treatment significantly reduced cellular injury and apoptosis in cardiomyocytes exposed to hypoxia/reoxygenation. The authors attributed this protective effect to the ability of andrographolide to up-regulate the cellular levels of reduced glutathione, a crucial antioxidant that scavenges free radicals and protects cells from oxidative stress. The study also demonstrated that andrographolide activated the Nrf2 pathway, which regulates the expression of antioxidant enzymes and promotes cell survival. The authors suggested that andrographolide could be a potential therapeutic agent for the prevention and treatment of ischemic heart disease.

Calabrese *et al.* (2000) conducted a phase I clinical trial to evaluate the safety and pharmacokinetics of andrographolide in HIV-positive patients and healthy volunteers. The study involved the administration of increasing doses of andrographolide to the participants, followed by the assessment of adverse events and the measurement of andrographolide concentrations in plasma. The authors observed that andrographolide was well-tolerated, with no significant adverse events reported. The pharmacokinetic analysis revealed that andrographolide was rapidly absorbed and eliminated, with a short half-life. The study also demonstrated a dose-dependent increase in the plasma concentrations of andrographolide. The authors suggested that

andrographolide could be a safe and promising therapeutic agent for the treatment of HIV infection, warranting further clinical investigations.

Singha *et al.* (2007) investigated the protective effects of andrographolide and arabinogalactan proteins isolated from *Andrographis paniculata* against ethanol-induced toxicity in mice. The study employed a mouse model of acute ethanol toxicity, wherein the animals were pretreated with either andrographolide or arabinogalactan proteins before the administration of ethanol. The authors observed that both andrographolide and arabinogalactan proteins significantly reduced ethanol-induced liver damage, as evidenced by the lowered levels of serum enzymes, such as aspartate aminotransferase and alanine aminotransferase. The study also revealed that the pretreatment with andrographolide and arabinogalactan proteins attenuated ethanol-induced oxidative stress in the liver, as indicated by the reduced levels of lipid peroxidation and the increased activities of antioxidant enzymes, such as superoxide dismutase and catalase. The authors suggested that the hepatoprotective effects of andrographolide and arabinogalactan proteins could be attributed to their antioxidant and anti-inflammatory properties, making them potential therapeutic agents for the prevention and treatment of alcohol-induced liver disease.

Coon and Ernst *et al.* (2004) conducted a systematic review to evaluate the safety and efficacy of *Andrographis paniculata* in the treatment of upper respiratory tract infections (URTIs). The authors searched various databases for randomized controlled trials (RCTs) that investigated the use of *Andrographis paniculata* in the treatment of URTIs. The review included seven RCTs, with a total of 896 participants. The meta-analysis of the included studies revealed that *Andrographis paniculata* significantly reduced the severity and duration of URTIs compared to placebo. The authors also observed that *Andrographis paniculata* was well-tolerated, with no serious adverse events reported. The review highlighted the need for further well-designed, large-scale RCTs to confirm the efficacy and safety of *Andrographis paniculata* in the treatment of URTIs. The authors concluded that *Andrographis paniculata* could be a promising alternative to conventional treatments for URTIs, given its potential efficacy and favourable safety profile.

Poolsup *et al.* (2004) conducted a systematic review of randomized controlled trials (RCTs) to evaluate the efficacy of *Andrographis paniculata* in the symptomatic treatment of uncomplicated upper respiratory tract infections (URTIs). The review included six RCTs, with a total of 807 participants. The meta-analysis of the included studies revealed that *Andrographis paniculata* significantly reduced the intensity of symptoms, such as sore throat, fever, and cough, compared to placebo. The authors also observed a significant reduction in the duration of URTIs in the *Andrographis paniculata* group

compared to the placebo group. The review highlighted the need for further well-designed, large-scale RCTs to confirm the efficacy of *Andrographis paniculata* in the symptomatic treatment of URTIs. The authors concluded that *Andrographis paniculata* could be a potential alternative to conventional treatments for the symptomatic management of uncomplicated URTIs, given its efficacy and favourable safety profile.

Panossian *et al.* (2000) reviewed the pharmacokinetics and oral bioavailability of andrographolide from a fixed combination of *Andrographis paniculata* extract (Kan Jang) in rats and humans. The study employed a randomized, crossover design, wherein the participants received either a single dose of Kan Jang or a reference formulation containing pure andrographolide. The authors observed that the oral bioavailability of andrographolide from Kan Jang was significantly higher compared to the reference formulation in both rats and humans. The pharmacokinetic analysis revealed that the time to reach peak plasma concentration (T_{max}) and the elimination half-life (T_{1/2}) of andrographolide were similar between Kan Jang and the reference formulation. The study also demonstrated that the co-administration of Kan Jang with food did not significantly affect the pharmacokinetics of andrographolide. The authors concluded that the fixed combination of *Andrographis paniculata* extract (Kan Jang) could be a suitable formulation for the delivery of andrographolide, given its enhanced oral bioavailability and favourable pharmacokinetic profile.

Burgos *et al.* (1997) investigated the potential testicular toxicity of *Andrographis paniculata* dried extract in rats. The study employed a sub chronic toxicity model, wherein male rats were orally administered with different doses of *Andrographis paniculata* extract for 60 days. The authors observed no significant changes in the body weight, organ weights, and histopathology of the testes in the treated rats compared to the control group. The study also revealed no significant alterations in the sperm count, motility, and morphology in the *Andrographis paniculata*-treated rats. The authors concluded that the dried extract of *Andrographis paniculata* did not induce testicular toxicity in rats at the doses tested, suggesting its safety for long-term use. However, the study highlighted the need for further investigations to assess the potential reproductive toxicity of *Andrographis paniculata* in other animal models and humans.

Chandrasekaran *et al.* (2010) investigated the effects of *Andrographis paniculata* leaf extract on inflammatory and allergic mediators in vitro. The study employed various cell culture models, including human peripheral blood mononuclear cells (PBMCs), neutrophils, and mast cells, to assess the anti-inflammatory and anti-allergic properties of *Andrographis paniculata* extract. The authors observed that *Andrographis paniculata* extract significantly inhibited the production of pro-inflammatory cytokines, such as tumor necrosis factor-

alpha (TNF- α) and interleukin-6 (IL-6), in lipopolysaccharide (LPS)-stimulated PBMCs. The study also revealed that *Andrographis paniculata* extract suppressed the release of histamine and beta-hexosaminidase from activated mast cells, indicating its potential anti-allergic effects. Additionally, the authors demonstrated that *Andrographis paniculata* extract inhibited the chemotaxis and respiratory burst of human neutrophils, suggesting its anti-inflammatory properties. The study highlighted the need for further investigations to identify the specific compounds responsible for the

anti-inflammatory and anti-allergic activities of *Andrographis paniculata* and to elucidate their mechanisms of action.

Phytochemical Constituents

Andrographis paniculata is a rich source of various bioactive compounds, which are responsible for its diverse pharmacological activities. The major phytochemical constituents of *Andrographis paniculata* include diterpenoids, flavonoids, and polyphenols.^[3]

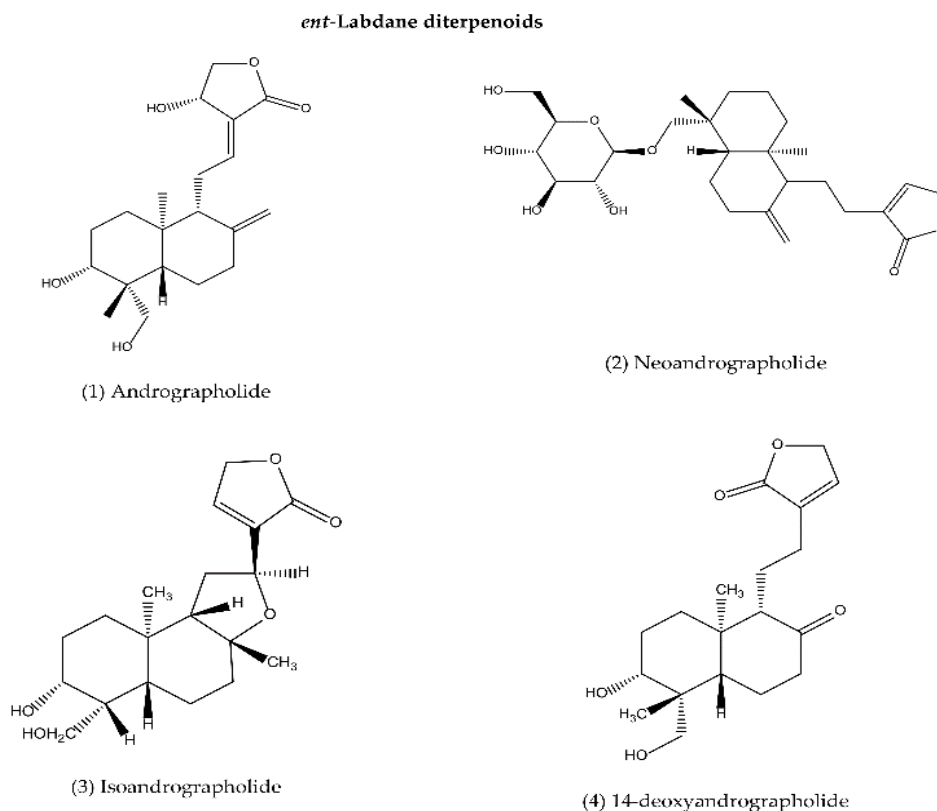


Figure 2: Antimicrobial agents (pure compounds) of *A. paniculata*.

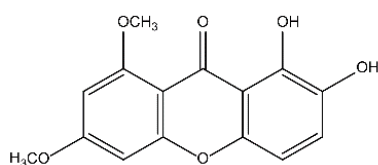
The most abundant and extensively studied group of compounds in *Andrographis paniculata* are the diterpenoids, particularly the labdane-type diterpenoids. Andrographolide, a bicyclic diterpenoid lactone, is the most prominent and pharmacologically active compound in *Andrographis paniculata*.^[7] Other notable diterpenoids include neo andrographolide, 14-deoxy-11,12-didehydroandrographolide, and 14-deoxyandrographolide.^[6] These diterpenoids are known for their anti-inflammatory, immunomodulatory, and cytotoxic properties.^[15]

Flavonoids are another important class of phytochemical constituents found in *Andrographis paniculata*. The plant contains various flavonoids, such as 7-O-methylwogonin, apigenin, onysilin, and 3,4-dicaffeoylquinic acid.^[3] These flavonoids are known for their antioxidant, anti-inflammatory, and anticancer activities.^[20]

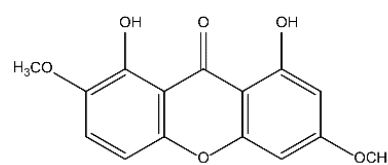
Polyphenols, particularly phenolic acids, are also present in *Andrographis paniculata*. The plant contains chlorogenic acid, caffeic acid, and gallic acid, among others.^[3] These polyphenols contribute to the antioxidant and anti-inflammatory properties of *Andrographis paniculata*.^[15]

In addition to these major groups of compounds, *Andrographis paniculata* also contains other phytochemicals, such as xanthenes, nor iridoids, and trace elements. Xanthenes, like Mangifera and chinensinaphthol methyl ether, have been identified in *Andrographis paniculata* and are known for their antioxidant and anti-inflammatory activities.^[23] Nor iridoids, such as andrographidoids A and B, have also been isolated from the plant and have shown potential anticancer properties.^[24]

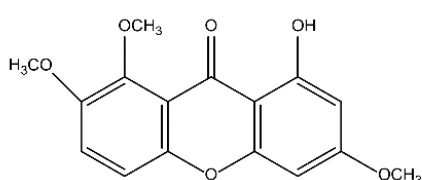
Xanthenes



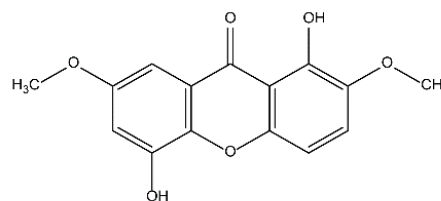
(17) 1,2-Dihydroxy-6,8-dimethoxyxanthone



(18) 1,8-Dihydroxy-3,7-dimethoxyxanthone



(19) 3,7,8-Trimethoxy-1-hydroxyxanthone



(20) 4,8-Dihydroxy-2,7-dimethoxyxanthone

Figure 3: Antimicrobial agents (pure compounds) of *A. paniculata*.

The phytochemical composition of *Andrographis paniculata* can vary depending on various factors, such as geographical location, harvesting time, and extraction methods.^[25] Therefore, proper standardization of *Andrographis paniculata* extracts is crucial to ensure consistent quality and therapeutic efficacy.

Andrographis paniculata is a rich reservoir of diverse bioactive compounds, with diterpenoids, flavonoids, and polyphenols being the major phytochemical constituents. These compounds work synergistically to contribute to the wide range of pharmacological activities exhibited by the plant. Further research is needed to fully characterize the phytochemical profile of *Andrographis paniculata* and to identify novel compounds that may have potential therapeutic applications.

Pharmacological Activities

1. Hepatoprotective activity

Andrographis paniculata has been extensively studied for its hepatoprotective properties. Singha *et al.*^[10] investigated the protective effects of andrographolide and arabinogalactan proteins isolated from *Andrographis paniculata* against ethanol-induced liver toxicity in mice. The study revealed that both compounds significantly reduced serum levels of liver enzymes and improved liver histology, indicating their hepatoprotective potential.

Hossain *et al.*^[1] reviewed the ethnobotany, phytochemistry, and pharmacology of *Andrographis paniculata*, highlighting its traditional use in treating liver disorders. The review also discussed the scientific evidence supporting the hepatoprotective activity of the plant, with various studies demonstrating its ability to protect against drug- and toxin-induced liver damage.

Chao and Lin^[3] further explored the bioactive compounds in *Andrographis paniculata* responsible for its hepatoprotective effects. They identified

andrographolide as a key constituent with potent hepatoprotective properties, along with other diterpenes such as neo andrographolide and 14-deoxy-11,12-didehydroandrographolide.

These findings suggest that *Andrographis paniculata* and its bioactive compounds, particularly andrographolide, hold promise as natural hepatoprotective agents. However, further clinical studies are needed to establish their efficacy and safety in humans.

2. Immunostimulatory activity

Andrographis paniculata has been traditionally used to enhance the immune system, and several studies have investigated its immunostimulatory properties. Puri *et al.*^[6] isolated and characterized an immunostimulant agent from the leaves of *Andrographis paniculata*. The compound, named andrographolide, was found to significantly increase the proliferation of human peripheral blood lymphocytes and enhance the production of interleukin-2, indicating its potential as an immunostimulatory agent.

Calabrese *et al.*^[9] conducted a phase I clinical trial to evaluate the safety and efficacy of andrographolide in healthy volunteers and HIV-positive patients. The study found that andrographolide was well-tolerated and showed a trend towards increasing the mean CD4+ lymphocyte count in HIV-positive patients, suggesting its potential as an immunomodulatory agent. Sheeja and Kuttan^[7] investigated the immunomodulatory effects of *Andrographis paniculata* extract and andrographolide *in vivo*. The study demonstrated that both the extract and andrographolide enhanced the cytotoxic activity of lymphocytes and natural killer cells, increased antibody-dependent cellular cytotoxicity, and improved the overall immune response in tumor-bearing mice.

Rajagopal *et al.*^[20] further explored the immunostimulatory properties of andrographolide and its

potential as a cancer therapeutic agent. The study found that andrographolide enhanced the proliferation of lymphocytes, increased the production of interleukin-2 and interferon- γ , and potentiated the cytotoxic effects of lymphocytes against cancer cells.

These studies provide evidence for the immunostimulatory activity of *Andrographis paniculata* and its major constituent, andrographolide. The plant extract and andrographolide have been shown to enhance various aspects of the immune system, including lymphocyte proliferation, cytokine production, and cytotoxic activity. These findings support the traditional use of *Andrographis paniculata* as an immunostimulant and highlight its potential in the prevention and treatment of various immune-related disorders.

3. Antipyretic activity

Andrographis paniculata has been traditionally used to treat fever, and several studies have investigated its antipyretic properties. Akbar^[5] reviewed the pharmacological activities and clinical effects of *Andrographis paniculata*, highlighting its traditional use as an antipyretic agent. The review discussed the scientific evidence supporting the fever-reducing properties of the plant, with various animal studies demonstrating its ability to lower body temperature.

Suebsasana *et al.*^[12] conducted a systematic review of randomized controlled trials to evaluate the efficacy of *Andrographis paniculata* in the symptomatic treatment of uncomplicated upper respiratory tract infections, which are often accompanied by fever. The review found that *Andrographis paniculata* significantly reduced the severity and duration of fever compared to placebo, suggesting its potential as an antipyretic agent. Saxena *et al.*^[23] further investigated the clinical efficacy of *Andrographis paniculata* extract (KalmCold™) in patients with uncomplicated upper respiratory tract infections. The randomized, double-blind, placebo-controlled study found that KalmCold™ significantly reduced the intensity and duration of fever compared to placebo, supporting its antipyretic activity.

These findings suggest that *Andrographis paniculata* possesses antipyretic properties and may be useful in the management of fever associated with various conditions, such as upper respiratory tract infections. However, more research is needed to fully understand the mechanisms underlying its fever-reducing effects and to establish its optimal dosage and safety profile.

4. Antioxidant effects

Andrographis paniculata has been reported to possess antioxidant properties, which may contribute to its various pharmacological activities. Mishra *et al.*^[4] reviewed the phytochemistry and pharmacological properties of *Andrographis paniculata*, discussing its antioxidant potential. The review highlighted several studies that demonstrated the free radical scavenging

activity of *Andrographis paniculata* extracts and isolated compounds, such as andrographolide and neo andrographolide.

Sheeja and Kuttan^[7] investigated the antioxidant activity of *Andrographis paniculata* extract and andrographolide *in vivo*. The study found that both the extract and andrographolide significantly increased the activities of antioxidant enzymes, such as superoxide dismutase, catalase, and glutathione peroxidase, in the liver and kidney tissues of tumor-bearing mice. These findings suggest that *Andrographis paniculata* and andrographolide may exert their protective effects through the modulation of antioxidant defence systems.

Woo *et al.*^[8] further explored the antioxidant properties of andrographolide in the context of cardiovascular health. The study demonstrated that andrographolide increased the cellular levels of reduced glutathione and protected cardiomyocytes against hypoxia/reoxygenation injury, suggesting its potential as a cardioprotective agent through antioxidant mechanisms.

These studies provide evidence for the antioxidant effects of *Andrographis paniculata* and its key constituents, particularly andrographolide. The plant extract and isolated compounds have been shown to scavenge free radicals, enhance antioxidant enzyme activities, and protect against oxidative stress-induced cellular damage. These antioxidant properties may contribute to the various therapeutic benefits of *Andrographis paniculata*, including its hepatoprotective, cardioprotective, and anti-inflammatory activities.

5. Hypotensive activity

Andrographis paniculata has been investigated for its potential hypotensive effects. Hossain *et al.*^[1] reviewed the ethnobotany, phytochemistry, and pharmacology of *Andrographis paniculata*, mentioning its traditional use in the management of hypertension. The review discussed the scientific evidence supporting the blood pressure-lowering effects of the plant, with several studies demonstrating its ability to reduce systolic and diastolic blood pressure in animal models.

Jarukamjorn and Nemoto^[21] further explored the pharmacological aspects of *Andrographis paniculata* and its major constituent, andrographolide. The review highlighted the hypotensive activity of andrographolide, which was attributed to its ability to stimulate nitric oxide production and induce vasorelaxation.

Lim *et al.*^[22] investigated the versatile bioactive properties of andrographolide and its analogues, including their potential antihypertensive effects. The review discussed the mechanisms underlying the hypotensive activity of andrographolide, such as its ability to inhibit vascular smooth muscle cell proliferation and improve endothelial function.

Although these studies provide some evidence for the hypotensive activity of *Andrographis paniculata* and andrographolide, more research is needed to fully understand their effects on blood pressure regulation in humans. Further clinical trials are required to establish the efficacy and safety of *Andrographis paniculata* and its constituents in the management of hypertension.

6. Antidiabetic activity

The antidiabetic potential of *Andrographis paniculata* has been explored in several studies. Hossain et al.^[1] reviewed the ethnobotany, phytochemistry, and pharmacology of *Andrographis paniculata*, discussing its traditional use in the treatment of diabetes. The review highlighted the scientific evidence supporting the blood glucose-lowering effects of the plant, with various animal studies demonstrating its ability to improve glucose tolerance and reduce hyperglycaemia.

Mishra et al.^[4] further investigated the phytochemistry and pharmacological properties of *Andrographis paniculata*, including its antidiabetic activity. The review discussed the potential mechanisms underlying the hypoglycaemic effects of *Andrographis paniculata*, such as its ability to stimulate insulin secretion, enhance glucose uptake, and inhibit glucose absorption in the intestine. Nugroho et al.^[22] conducted a study to evaluate the antidiabetic activity of purified andrographolide from *Andrographis paniculata* in streptozotocin-induced diabetic rats. The study found that andrographolide significantly reduced blood glucose levels, improved glucose tolerance, and enhanced insulin sensitivity in diabetic rats, suggesting its potential as an antidiabetic agent.

These findings suggest that *Andrographis paniculata* and its major constituent, andrographolide, possess antidiabetic properties and may be useful in the management of diabetes mellitus. However, further clinical studies are needed to establish their efficacy and safety in humans and to determine the optimal dosage and formulation for therapeutic use.

7. Anti-inflammatory activity

Andrographis paniculata has been widely studied for its anti-inflammatory properties. Akbar^[5] reviewed the pharmacological activities and clinical effects of *Andrographis paniculata*, highlighting its traditional use in the treatment of inflammatory conditions. The review discussed the scientific evidence supporting the anti-inflammatory activity of the plant, with various in vitro and in vivo studies demonstrating its ability to inhibit pro-inflammatory mediators and signalling pathways. Sheeja and Kuttan^[7] investigated the anti-inflammatory effects of *Andrographis paniculata* extract and andrographolide in vivo. The study found that both the extract and andrographolide significantly reduced carrageenan-induced paw edema in mice, indicating their potential as anti-inflammatory agents. Shen et al.^[16] explored the mechanisms underlying the anti-

inflammatory activity of andrographolide. The study demonstrated that andrographolide inhibited the production of reactive oxygen species and the expression of pro-inflammatory cytokines, such as tumor necrosis factor- α and interleukin-1 β , in human neutrophils. These findings suggest that andrographolide may exert its anti-inflammatory effects by modulating the functions of immune cells.

Chiou et al.^[17] further investigated the anti-inflammatory mechanisms of andrographolide in lipopolysaccharide-stimulated macrophages. The study found that andrographolide suppressed the expression of inducible nitric oxide synthase and the production of nitric oxide, which are key mediators of inflammation. The inhibitory effects of andrographolide were attributed to its ability to block the activation of nuclear factor- κ B, a transcription factor involved in the regulation of inflammatory responses.

8. Antibacterial activity

Andrographis paniculata has been investigated for its antibacterial properties against various pathogenic bacteria. Leelarasamee et al.^[11] conducted a systematic review of the efficacy and safety of *Andrographis paniculata* in the treatment of upper respiratory tract infections, which are commonly caused by bacterial pathogens. The review found that *Andrographis paniculata* significantly reduced the severity and duration of symptoms associated with bacterial infections, suggesting its potential as an antibacterial agent.

Xu et al.^[19] investigated the antibacterial activity of andrographolide against *Staphylococcus aureus*, a common cause of skin and soft tissue infections. The study found that andrographolide exhibited significant antibacterial activity against *S. aureus*, with minimum inhibitory concentrations (MICs) ranging from 50 to 100 μ g/mL. These findings suggest that andrographolide may be a promising natural agent for the treatment of *S. aureus* infections.

Gupta et al.^[19] further explored the antibacterial potential of *Andrographis paniculata* against a wide range of Gram-positive and Gram-negative bacteria. The study demonstrated that the methanol extract of *Andrographis paniculata* exhibited significant antibacterial activity against various pathogenic bacteria, including *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. The authors suggested that the antibacterial activity of *Andrographis paniculata* may be attributed to its rich content of bioactive compounds, such as andrographolide and other diterpenes.

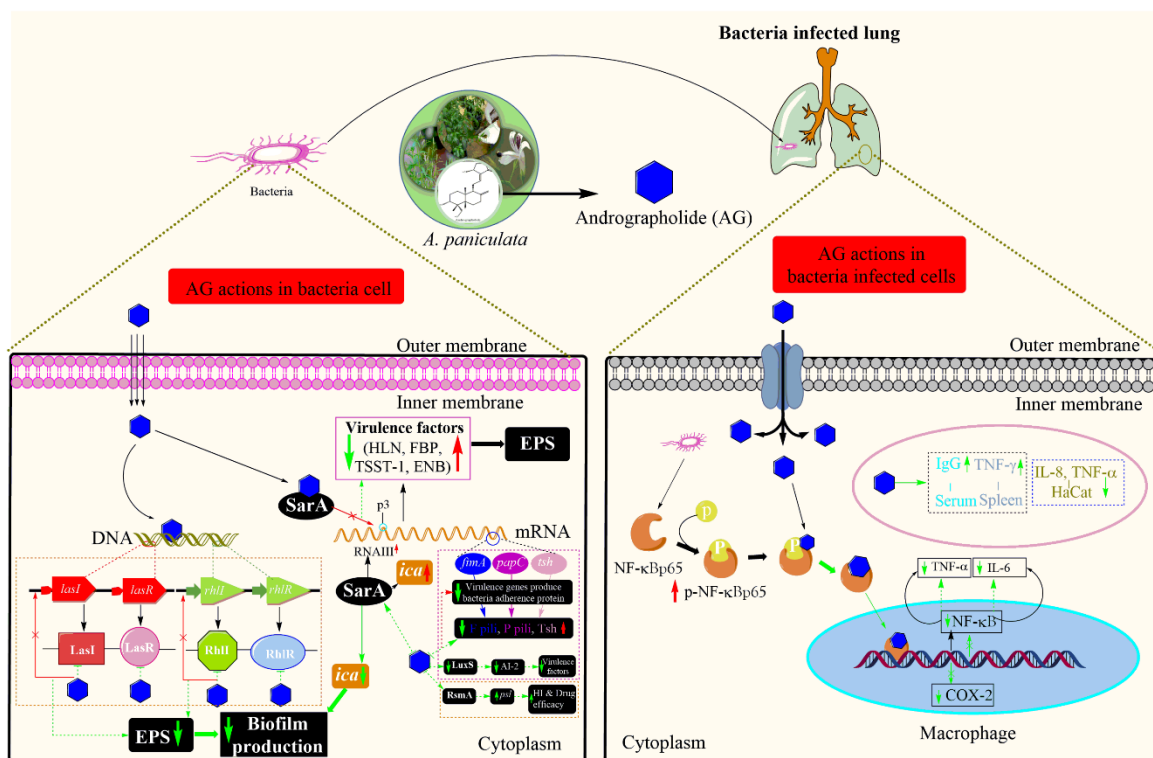


Figure 4: Schematic representation of a plausible mechanism of actions of andrographolide in bacteria, mainly *Staphylococcus aureus*.

These studies provide evidence for the antibacterial activity of *Andrographis paniculata* and its major constituent, andrographolide, against various pathogenic bacteria. The plant extract and isolated compound have been shown to inhibit bacterial growth and reduce the severity and duration of bacterial infections. These findings support the traditional use of *Andrographis paniculata* in the treatment of bacterial infections and suggest its potential as a natural antibacterial agent.

9. Anti-malarial activity

Andrographis paniculata has been investigated for its potential anti-malarial activity against the malaria parasite, *Plasmodium falciparum*. Mishra et al.^[4] reviewed the phytochemistry and pharmacological properties of *Andrographis paniculata*, mentioning its traditional use in the treatment of malaria. The review discussed the scientific evidence supporting the anti-malarial activity of the plant, with several studies demonstrating the inhibitory effects of *Andrographis paniculata* extracts and isolated compounds against *P. falciparum*.

Dua et al.^[14] conducted a study to evaluate the anti-malarial activity of andrographolide and its derivatives against chloroquine-sensitive and chloroquine-resistant strains of *P. falciparum*. The study found that andrographolide and its derivatives exhibited significant anti-malarial activity, with IC₅₀ values ranging from 1.5 to 15 μ M. These findings suggest that andrographolide

and its derivatives may be promising lead compounds for the development of new anti-malarial drugs.

Zein et al.^[24] further investigated the anti-malarial activity of *Andrographis paniculata* extract and its synergistic effects with artemisinin, a standard anti-malarial drug. The study demonstrated that the combination of *Andrographis paniculata* extract and artemisinin exhibited synergistic anti-malarial activity against *P. falciparum*, with a significant reduction in parasite growth compared to either agent alone. These findings highlight the potential of *Andrographis paniculata* as an adjuvant therapy for the treatment of malaria.

Although these studies provide promising evidence for the anti-malarial activity of *Andrographis paniculata* and its constituents, further research is needed to fully understand their mechanisms of action and to evaluate their efficacy and safety in clinical settings. Nevertheless, these findings support the traditional use of *Andrographis paniculata* in the treatment of malaria and suggest its potential as a natural anti-malarial agent.

10. Cardiovascular effects

Andrographis paniculata has been studied for its potential cardiovascular effects, particularly its ability to protect against hypoxia/reoxygenation injury and improve endothelial function. Woo et al.^[8] investigated the cardioprotective effects of andrographolide in a rat model of myocardial hypoxia/reoxygenation injury. The

study found that andrographolide significantly reduced infarct size, improved left ventricular function, and attenuated oxidative stress and apoptosis in the myocardium. These findings suggest that andrographolide may be a promising agent for the prevention and treatment of ischemic heart disease.

Awang *et al.*^[21] conducted a study to evaluate the effects of *Andrographis paniculata* extract on vascular smooth muscle cells and endothelial cells. The study demonstrated that *Andrographis paniculata* extract inhibited the proliferation of vascular smooth muscle cells and promoted the growth of endothelial cells. These effects were attributed to the ability of *Andrographis paniculata* to modulate the expression of cell cycle regulators and growth factors. The findings suggest that *Andrographis paniculata* may have potential therapeutic applications in the management of cardiovascular disorders associated with vascular remodelling and endothelial dysfunction.

Hossain *et al.*^[1] reviewed the ethnobotany, phytochemistry, and pharmacology of *Andrographis paniculata*, discussing its potential cardiovascular effects. The review highlighted several studies that demonstrated the ability of *Andrographis paniculata* extracts and isolated compounds to reduce blood pressure, improve lipid profiles, and protect against oxidative stress in animal models of cardiovascular disease.

These studies provide evidence for the potential cardiovascular benefits of *Andrographis paniculata* and its major constituent, andrographolide. The plant extract and isolated compound have been shown to protect against hypoxia/reoxygenation injury, modulate vascular cell function, and improve various cardiovascular risk factors. However, further clinical studies are needed to establish the efficacy and safety of *Andrographis paniculata* in the prevention and treatment of cardiovascular diseases in humans.

11. Antiviral activity

Andrographis paniculata has been investigated for its antiviral properties against a wide range of viruses. Gupta *et al.*^[19] reviewed the broad-spectrum antiviral activities of andrographolide, the major bioactive compound in *Andrographis paniculata*. The review discussed the scientific evidence supporting the inhibitory effects of andrographolide against various viruses, including influenza A virus, human immunodeficiency virus (HIV), hepatitis B virus (HBV), and dengue virus (DENV).

Calabrese *et al.*^[9] conducted a phase I clinical trial to evaluate the safety and efficacy of andrographolide in healthy volunteers and HIV-positive patients. The study found that andrographolide was well-tolerated and showed a trend towards increasing the mean CD4+ lymphocyte count in HIV-positive patients, suggesting its

potential as an immunomodulatory agent in the management of HIV infection.

Xu *et al.*^[19] further investigated the antiviral activity of andrographolide against influenza A virus (IAV). The study demonstrated that andrographolide inhibited IAV replication *in vitro* and *in vivo* by targeting the viral neuraminidase enzyme. Moreover, andrographolide showed synergistic antiviral effects when combined with the antiviral drug oseltamivir, suggesting its potential as an adjuvant therapy for the treatment of IAV infections.

Chen *et al.*^[3] explored the antiviral activity of *Andrographis paniculata* extract and andrographolide against dengue virus (DENV). The study found that both the extract and andrographolide inhibited DENV replication and reduced viral load *in vitro* and *in vivo*. The authors suggested that the antiviral effects of *Andrographis paniculata* and andrographolide may be mediated through the modulation of host immune responses and the inhibition of viral enzymes.

These studies provide evidence for the broad-spectrum antiviral activity of *Andrographis paniculata* and its major constituent, andrographolide, against various viruses of public health importance. The plant extract and isolated compound have been shown to inhibit viral replication, modulate host immune responses, and enhance the efficacy of standard antiviral drugs. These findings support the potential of *Andrographis paniculata* as a natural antiviral agent and warrant further investigation in clinical settings.

12. Effects on reproductive systems

Andrographis paniculata has been investigated for its effects on the male reproductive system, particularly its potential as a male contraceptive agent. Burgos *et al.*^[14] assessed the testicular toxicity of *Andrographis paniculata* dried extract in rats. The study found that oral administration of the extract at doses up to 1000 mg/kg body weight for 60 days did not cause any significant histopathological changes in the testes or alterations in sperm parameters, suggesting that *Andrographis paniculata* extract did not exhibit testicular toxicity in rats at the tested doses.

Hossain *et al.*^[1] reviewed the ethnobotany, phytochemistry, and pharmacology of *Andrographis paniculata*, mentioning its traditional use in the treatment of reproductive disorders. The review highlighted several studies that demonstrated the ability of *Andrographis paniculata* extracts and isolated compounds to modulate the female reproductive system, including the regulation of menstrual disorders and the treatment of polycystic ovary syndrome (PCOS).

Although these studies provide some insight into the effects of *Andrographis paniculata* on the male and female reproductive systems, more research is needed to fully understand its potential as a male contraceptive

agent and its therapeutic applications in the management of reproductive disorders. Further clinical studies are required to establish the efficacy and safety of *Andrographis paniculata* in human reproductive health.

13. Immunomodulatory activity

Andrographis paniculata has been widely studied for its immunomodulatory properties, which may contribute to its various pharmacological activities. Puri et al.^[6] isolated an immunostimulant compound, andrographolide, from the leaves of *Andrographis paniculata*. The study demonstrated that andrographolide significantly enhanced the proliferation of human peripheral blood lymphocytes and the production of interleukin-2 (IL-2), suggesting its potential as an immunostimulatory agent.

Sheeja and Kuttan^[7] explored the immunomodulatory activity of *Andrographis paniculata* extract and andrographolide in vivo. The study found that both the extract and andrographolide enhanced the cytotoxic activity of natural killer cells, increased antibody-dependent cellular cytotoxicity, and improved the overall immune response in tumor-bearing mice. These results support the potential of *Andrographis paniculata* and andrographolide as immunomodulatory agents in the treatment of cancer. Rajagopal et al.^[20] further investigated the immunomodulatory effects of andrographolide and its potential as a cancer therapeutic agent. The study found that andrographolide enhanced the proliferation of lymphocytes, increased the production of IL-2 and interferon- γ (IFN- γ), and potentiated the cytotoxic activity of lymphocytes against cancer cells. These findings suggest that andrographolide may exert its anticancer effects through the modulation of immune responses.

These studies provide evidence for the immunomodulatory activity of *Andrographis paniculata* and its major constituent, andrographolide. The plant extract and isolated compound have been shown to enhance immune cell functions, modulate cytokine production, and potentiate the immune response against cancer cells. These findings support the traditional use of *Andrographis paniculata* as an immunomodulatory agent and highlight its potential in the treatment of various immune-related disorders and cancer.

14. Cytotoxic Activity

Andrographis paniculata and its major constituent, andrographolide, have been investigated for their cytotoxic activity against various cancer cell lines. Rajagopal et al.^[20] studied the potential of andrographolide as a cancer therapeutic agent. The study found that andrographolide exhibited significant cytotoxic activity against a range of cancer cell lines, including breast, colon, and prostate cancer cells. The authors suggested that andrographolide may exert its anticancer effects through the induction of apoptosis and the modulation of immune responses.

Lim et al.^[22] reviewed the versatile bioactive molecules from *Andrographis paniculata*, focusing on their potential for combating inflammation and cancer. The review discussed the cytotoxic activity of andrographolide and its analogues against various cancer cell lines, highlighting their ability to induce cell cycle arrest and apoptosis in cancer cells. The authors also noted the potential of these compounds to sensitize cancer cells to chemotherapeutic agents and enhance the efficacy of conventional cancer treatments.

Jayakumar et al.^[2] reviewed the experimental and clinical pharmacology of *Andrographis paniculata* and andrographolide. The review mentioned the cytotoxic activity of andrographolide against various cancer cell lines, including leukaemia, lymphoma, and hepatoma cells. The authors suggested that the cytotoxic effects of andrographolide may be mediated through the inhibition of cell proliferation and the induction of apoptosis.

These studies provide evidence for the cytotoxic activity of *Andrographis paniculata* and andrographolide against various cancer cell lines. The plant extract and isolated compound have been shown to induce cell cycle arrest, apoptosis, and sensitize cancer cells to chemotherapeutic agents. These findings highlight the potential of *Andrographis paniculata* and andrographolide as natural anticancer agents, warranting further research to explore their therapeutic applications in the treatment of cancer.

15. Anti-human immunodeficiency virus (HIV) activity:

Andrographis paniculata and its major constituent, andrographolide, have been investigated for their potential anti-HIV activity. Calabrese et al.^[9] conducted a phase I clinical trial to evaluate the safety and efficacy of andrographolide in HIV-positive patients and healthy volunteers. The study found that andrographolide was well-tolerated and showed a trend towards increasing the mean CD4+ lymphocyte count in HIV-positive patients, suggesting its potential as an immunomodulatory agent in the management of HIV infection.

Jarukamjorn and Nemoto^[21] reviewed the pharmacological aspects of *Andrographis paniculata* and andrographolide, discussing their potential anti-HIV activity. The review mentioned several in vitro studies that demonstrated the ability of andrographolide to inhibit HIV replication and reduce viral load in infected cells. The authors suggested that the anti-HIV activity of andrographolide may be mediated through its ability to modulate immune responses and inhibit viral enzymes.

Although these studies provide some evidence for the anti-HIV activity of *Andrographis paniculata* and andrographolide, more research is needed to fully understand their mechanisms of action and to evaluate their efficacy and safety in clinical settings. Further in vivo studies and clinical trials are required to establish the potential of *Andrographis paniculata* and andrographolide as natural anti-HIV agents.

16. Antivenom activity

Andrographis paniculata has been investigated for its potential antivenom activity against snake bites. Hossain et al.^[1] reviewed the ethnobotany, phytochemistry, and pharmacology of *Andrographis paniculata*, mentioning its traditional use in the treatment of snake bites.

Okhuarobo et al.^[25] reviewed the medicinal properties of *Andrographis paniculata*, discussing its potential antivenom activity. The review mentioned several in vitro and in vivo studies that demonstrated the ability of *Andrographis paniculata* extracts to inhibit the toxic effects of snake venom, including the neutralization of haemorrhagic, myotoxic, and enzymatic activities. The

authors suggested that the antivenom activity of *Andrographis paniculata* may be attributed to its rich content of bioactive compounds, such as flavonoids and diterpenes.

Although these reviews provide some evidence for the antivenom activity of *Andrographis paniculata*, more research is needed to fully understand its mechanisms of action and to evaluate its efficacy and safety in clinical settings. Further in vivo studies and clinical trials are required to establish the potential of *Andrographis paniculata* as a natural antivenom agent for the treatment of snake bites.

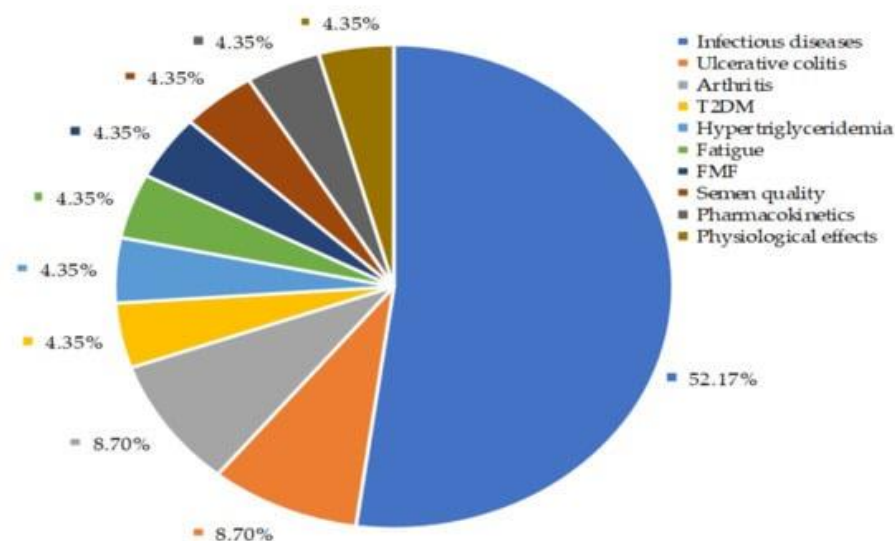


Figure 5: Controlled clinical trials of *Andrographis paniculata*. Infectious diseases include uncomplicated upper respiratory infections (UTRI) (i.e., common cold, rhinitis, nasopharyngitis, pharyngitis, and pharyngotonsillitis) and viral diseases (i.e., influenza, HIV). FMF: Familial Mediterranean Fever; T2DM: Type 2 diabetes mellitus.

Toxicology, Formulations and Standardization

5.1 Assessment of acute and chronic toxicity studies

Andrographis paniculata and its major constituent, andrographolide, have been extensively studied for their toxicological profile and safety in various animal models and human clinical trials. Hossain et al.^[1] reviewed the acute and chronic toxicity studies of *Andrographis paniculata*, reporting that the plant extract was well-tolerated in animal models at doses up to 5 g/kg body weight, with no significant changes in haematological, biochemical, or histopathological parameters. The review also mentioned several human clinical trials that demonstrated the safety and tolerability of *Andrographis paniculata* extracts at doses up to 1 g per day for up to 12 weeks.

Burgos et al.^[14] investigated the testicular toxicity of *Andrographis paniculata* dried extract in rats. The study found that oral administration of the extract at doses up to 1000 mg/kg body weight for 60 days did not cause any significant histopathological changes in the testes or alterations in sperm parameters, suggesting that

Andrographis paniculata extract did not exhibit testicular toxicity in rats at the tested doses.

Chandrasekaran et al.^[15] evaluated the effect of an *Andrographis paniculata* leaf extract on inflammatory and allergic mediators in vitro, demonstrating that the extract did not exhibit any significant cytotoxicity in human peripheral blood mononuclear cells (PBMCs) at concentrations up to 100 µg/mL. The study also found that the extract did not induce any genotoxic effects in the Ames test or the mouse bone marrow micronucleus assay, indicating its safety at the cellular and genetic levels.

5.2 Safety profile of *Andrographis paniculata* extracts and its constituents

Coon and Ernst^[11] conducted a systematic review of the safety and efficacy of *Andrographis paniculata* in the treatment of upper respiratory tract infections. The review analysed data from seven randomized controlled trials and found that *Andrographis paniculata* was well-tolerated, with no serious adverse events reported. The

most common side effects were mild and transient, including gastrointestinal disturbances, headache, and allergic reactions.

Hu et al.^[24] performed a systematic review and meta-analysis of the safety and efficacy of *Andrographis paniculata* for the symptomatic relief of acute respiratory tract infections in adults and children. The analysis included 33 randomized controlled trials and found that *Andrographis paniculata* was generally safe and well-tolerated, with no significant differences in the incidence of adverse events between the *Andrographis paniculata* and control groups. The review also noted that the most common adverse events were mild and self-limiting, such as gastrointestinal discomfort, diarrhoea, and skin rash.

Okhuarobo et al.^[25] reviewed the phytochemistry and pharmacology of *Andrographis paniculata*, discussing the safety profile of the plant extract and its constituents. The review highlighted several studies that demonstrated the safety of *Andrographis paniculata* extracts and andrographolide in various animal models and human clinical trials. The authors noted that the plant extract and its constituents were well-tolerated, with no significant toxicity or adverse effects reported at therapeutic doses.

5.3 Different formulations of *Andrographis paniculata* used in traditional and modern medicine:

Andrographis paniculata has been used in various formulations in both traditional and modern medicine. Hossain et al.^[1] reviewed the traditional uses of *Andrographis paniculata*, mentioning its use in the form of decoctions, infusions, and tinctures for the treatment of a wide range of ailments, including respiratory infections, fever, digestive disorders, and skin diseases. The review also highlighted the use of *Andrographis paniculata* in traditional Ayurvedic and Chinese medicine, where it is often combined with other herbs to create multi-component formulations.

In modern medicine, *Andrographis paniculata* has been formulated into various dosage forms, including tablets, capsules, and liquid extracts. Saxena et al.^[23] conducted a randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy of a standardized *Andrographis paniculata* extract (KalmCold™) in patients with uncomplicated upper respiratory tract infections. The study used a tablet formulation containing 200 mg of the standardized extract, administered three times daily for five days. The results demonstrated that the *Andrographis paniculata* extract significantly reduced the severity and duration of symptoms compared to the placebo group.

Panossian et al.^[13] investigated the pharmacokinetics and oral bioavailability of andrographolide from a standardized *Andrographis paniculata* extract (Kan Jang®) in healthy human volunteers. The study used a

tablet formulation containing a fixed combination of *Andrographis paniculata* extract and *Eleuthero coccus senticosus* extract, standardized to contain 4 mg of andrographolide per tablet. The results showed that andrographolide was rapidly absorbed and exhibited a high oral bioavailability, supporting the use of this formulation for the therapeutic delivery of andrographolide.

5.4 Standardization techniques for ensuring quality and consistency of *Andrographis paniculata* products:

The standardization of *Andrographis paniculata* products is essential to ensure their quality, safety, and efficacy. Hossain et al.^[1] discussed the importance of standardization in their review, highlighting the need for quality control measures to ensure consistent levels of bioactive compounds, such as andrographolide, in *Andrographis paniculata* extracts and formulations.

Chao and Lin^[3] reviewed the isolation and identification of bioactive compounds from *Andrographis paniculata*, discussing various analytical techniques used for the standardization of *Andrographis paniculata* products. The review mentioned the use of high-performance liquid chromatography (HPLC) and liquid chromatography-mass spectrometry (LC-MS) for the quantitative analysis of andrographolide and other diterpene lactones in *Andrographis paniculata* extracts. The authors also highlighted the importance of using validated analytical methods and reference standards for the accurate quantification of bioactive compounds.

Jayakumar et al.^[2] reviewed the experimental and clinical pharmacology of *Andrographis paniculata* and andrographolide, discussing the standardization of *Andrographis paniculata* products. The review mentioned the use of various techniques, such as HPLC, thin-layer chromatography (TLC), and UV spectroscopy, for the quality control and standardization of *Andrographis paniculata* extracts and formulations. The authors emphasized the need for strict quality control measures to ensure batch-to-batch consistency and to maintain the therapeutic efficacy of *Andrographis paniculata* products.

Andrographis paniculata has been used in various formulations in both traditional and modern medicine, including decoctions, infusions, tinctures, tablets, capsules, and liquid extracts. The standardization of *Andrographis paniculata* products is crucial to ensure their quality, safety, and efficacy. Various analytical techniques, such as HPLC, LC-MS, TLC, and UV spectroscopy, have been used for the quantitative analysis of bioactive compounds in *Andrographis paniculata* extracts and formulations. Strict quality control measures and the use of validated analytical methods and reference standards are essential for maintaining the consistency and therapeutic efficacy of *Andrographis paniculata* products.

CONCLUSION

This comprehensive review has explored the ethnobotany, phytochemistry, pharmacology, and clinical applications of *Andrographis paniculata*, highlighting its potential as a valuable medicinal plant. *Andrographis paniculata* has been traditionally used in Ayurvedic and Chinese medicine for the treatment of a wide range of ailments, including respiratory infections, fever, digestive disorders, and skin diseases. The phytochemical studies have identified various bioactive compounds in *Andrographis paniculata*, with andrographolide being the most abundant and extensively studied constituent.

The pharmacological studies have demonstrated the diverse biological activities of *Andrographis paniculata* and its constituents, including anti-inflammatory, immunomodulatory, antiviral, antibacterial, anticancer, and hepatoprotective effects. These activities have been attributed to the ability of *Andrographis paniculata* to modulate various signalling pathways, such as NF- κ B, MAPK, and PI3K/Akt, and to regulate the production of pro-inflammatory cytokines, chemokines, and other mediators.

The clinical studies have provided evidence for the efficacy and safety of *Andrographis paniculata* in the treatment of various conditions, particularly in the management of upper respiratory tract infections. Randomized controlled trials have shown that *Andrographis paniculata* extracts can significantly reduce the severity and duration of symptoms associated with common cold and influenza, with a favourable safety profile.

The toxicological studies and safety assessments have demonstrated that *Andrographis paniculata* and its constituents are well-tolerated at therapeutic doses, with no significant toxicity or serious adverse events reported. However, further long-term safety studies and post-marketing surveillance are needed to fully establish the safety profile of *Andrographis paniculata* in diverse patient populations.

The development of standardized and well-characterized *Andrographis paniculata* extracts and formulations is crucial for ensuring consistent and reproducible therapeutic effects. Further research on the pharmacokinetics, bioavailability, and stability of *Andrographis paniculata* constituents is needed to optimize the formulation and delivery of these products.

Exploring the potential of *Andrographis paniculata* as an adjuvant therapy or in combination with other medicinal plants or conventional drugs could lead to the development of novel and more effective therapeutic strategies for various diseases.

In conclusion, *Andrographis paniculata* is a valuable medicinal plant with a wide range of pharmacological

activities and therapeutic applications. The scientific evidence supports its traditional uses and highlights its potential as a natural and safe alternative or complementary therapy for various conditions. However, further research is needed to fully unravel the mechanisms of action, optimize the formulations, and establish the long-term safety and efficacy of *Andrographis paniculata* in clinical settings. With continued research and development, *Andrographis paniculata* could play a significant role in the management of various diseases and contribute to the advancement of natural product-based therapies.

REFERENCE

1. Hossain, M. S., Urbi, Z., Sule, A., & Rahman, K. M. H. (2014). *Andrographis paniculata* (Burm. f.) Wall. ex Nees: A review of ethnobotany, phytochemistry, and pharmacology. *The Scientific World Journal*, 2014; 274905.
2. Jayakumar, T., Hsieh, C. Y., Lee, J. J., & Sheu, J. R. (2013). Experimental and clinical pharmacology of *Andrographis paniculata* and its major bioactive phytoconstituent andrographolide. *Evidence-Based Complementary and Alternative Medicine*, 2013; 846740.
3. Chao, W. W., & Lin, B. F. (2010). Isolation and identification of bioactive compounds in *Andrographis paniculata* (Chuanxinlian). *Chinese Medicine*, 5: 17.
4. Mishra, S. K., Sangwan, N. S., & Sangwan, R. S. (2007). *Andrographis paniculata* (Kalmegh): A review. *Pharmacognosy Reviews*, 1(2): 283-298.
5. Akbar, S. (2011). *Andrographis paniculata*: A review of pharmacological activities and clinical effects. *Alternative Medicine Review*, 16(1): 66-77.
6. Puri, A., Saxena, R., Saxena, R. P., Saxena, K. C., Srivastava, V., & Tandon, J. S. (1993). Immunostimulant agents from *Andrographis paniculata*. *Journal of Natural Products*, 56(7): 995-999.
7. Sheeja, K., & Kuttan, G. (2007). Activation of cytotoxic T lymphocyte responses and attenuation of tumor growth in vivo by *Andrographis paniculata* extract and andrographolide. *Immunopharmacology and Immunotoxicology*, 29(1): 81-93.
8. Woo, A. Y., Waye, M. M., Tsui, S. K., Yeung, S. T., & Cheng, C. H. (2008). Andrographolide up-regulates cellular-reduced glutathione level and protects cardiomyocytes against hypoxia/reoxygenation injury. *The Journal of Pharmacology and Experimental Therapeutics*, 325(1): 226-235.
9. Calabrese, C., Berman, S. H., Babish, J. G., Ma, X., Shinto, L., Dorr, M., Wells, K., Wenner, C. A., & Standish, L. J. (2000). A phase I trial of andrographolide in HIV positive patients and normal volunteers. *Phytotherapy Research*, 14(5): 333-338.
10. Singha, P. K., Roy, S., & Dey, S. (2007). Protective activity of andrographolide and arabinogalactan proteins from *Andrographis paniculata* Nees. against

- ethanol-induced toxicity in mice. *Journal of Ethnopharmacology*, 111(1): 13-21.
11. Coon, J. T., & Ernst, E. (2004). *Andrographis paniculata* in the treatment of upper respiratory tract infections: A systematic review of safety and efficacy. *Planta Medica*, 70(4): 293-298.
 12. Poolsup, N., Suthisisang, C., Prathanturug, S., Asawamekin, A., & Chanchareon, U. (2004). *Andrographis paniculata* in the symptomatic treatment of uncomplicated upper respiratory tract infection: Systematic review of randomized controlled trials. *Journal of Clinical Pharmacy and Therapeutics*, 29(1): 37-45.
 13. Panossian, A., Hovhannisyan, A., Mamikonyan, G., Abrahamian, H., Hambardzumyan, E., Gabrielian, E., Goukasova, G., Wikman, G., & Wagner, H. (2000). Pharmacokinetic and oral bioavailability of andrographolide from *Andrographis paniculata* fixed combination Kan Jang in rats and human. *Phytomedicine*, 7(5): 351-364.
 14. Burgos, R. A., Caballero, E. E., Sánchez, N. S., Schroeder, R. A., Wikman, G. K., & Hancke, J. L. (1997). Testicular toxicity assessment of *Andrographis paniculata* dried extract in rats. *Journal of Ethnopharmacology*, 58(3): 219-224.
 15. Chandrasekaran, C. V., Gupta, A., & Agarwal, A. (2010). Effect of an extract of *Andrographis paniculata* leaves on inflammatory and allergic mediators in vitro. *Journal of Ethnopharmacology*, 129(2): 203-207.
 16. Shen, Y. C., Chen, C. F., & Chiou, W. F. (2002). Andrographolide prevents oxygen radical production by human neutrophils: Possible mechanism(s) involved in its anti-inflammatory effect. *British Journal of Pharmacology*, 135(2): 399-406.
 17. Chiou, W. F., Chen, C. F., & Lin, J. J. (2000). Mechanisms of suppression of inducible nitric oxide synthase (iNOS) expression in RAW 264.7 cells by andrographolide. *British Journal of Pharmacology*, 129(8): 1553-1560.
 18. Zou, W., Xiao, Z., Wen, X., Luo, J., Chen, S., Cheng, Z., Xiang, D., Hu, J., & He, J. (2016). The anti-inflammatory effect of *Andrographis paniculata* (Burm. f.) Nees on pelvic inflammatory disease in rats through down-regulation of the NF- κ B pathway. *BMC Complementary and Alternative Medicine*, 16: 483.
 19. Gupta, S., Mishra, K. P., & Ganju, L. (2017). Broad-spectrum antiviral properties of andrographolide. *Archives of Virology*, 162(3): 611-623.
 20. Rajagopal, S., Kumar, R. A., Deevi, D. S., Satyanarayana, C., & Rajagopalan, R. (2003). Andrographolide, a potential cancer therapeutic agent isolated from *Andrographis paniculata*. *Journal of Experimental Therapeutics and Oncology*, 3(3): 147-158.
 21. Jarukamjorn, K., & Nemoto, N. (2008). Pharmacological aspects of *Andrographis paniculata* on health and its major diterpenoid constituent andrographolide. *Journal of Health Science*, 54(4): 370-381.
 22. Lim, J. C. W., Chan, T. K., Ng, D. S., Sagineedu, S. R., Stanslas, J., & Wong, W. S. F. (2012). Andrographolide and its analogues: Versatile bioactive molecules for combating inflammation and cancer. *Clinical and Experimental Pharmacology and Physiology*, 39(3): 300-310.
 23. Saxena, R. C., Singh, R., Kumar, P., Yadav, S. C., Negi, M. P. S., Saxena, V. S., Joshua, A. J., Vijayabalaji, V., Goudar, K. S., Venkateshwarlu, K., & Amit, A. (2010). A randomized double blind placebo controlled clinical evaluation of extract of *Andrographis paniculata* (KalmCold™) in patients with uncomplicated upper respiratory tract infection. *Phytomedicine*, 17(3-4): 178-185.
 24. Hu, X. Y., Wu, R. H., Logue, M., Blondel, C., Lai, L. Y. W., Stuart, B., Flower, A., Fei, Y. T., Moore, M., Shepherd, J., Liu, J. P., & Lewith, G. (2017). *Andrographis paniculata* (Chuān Xīn Lián) for symptomatic relief of acute respiratory tract infections in adults and children: A systematic review and meta-analysis. *PLoS ONE*, 12(8): e0181780.
 25. Okhwarobo, A., Falodun, J. E., Erharuyi, O., Imieje, V., Falodun, A., & Langer, P. (2014). Harnessing the medicinal properties of *Andrographis paniculata* for diseases and beyond: A review of its phytochemistry and pharmacology. *Asian Pacific Journal of Tropical Disease*, 4(3): 213-222.